REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 168-189 are in the case.

I. ELECTION/RESTRICTION

The election of Group II, claims 141-167, and the species of claim 153 wherein M is H is acknowledged. New claims 168-189 presented herewith read on the elected species.

The comment appearing in the first paragraph on page 3 of the Action has been noted. The prior claims have been replaced by new claims 168-189.

II. THE WRITTEN DESCRIPTION REJECTION

Claims 141-148, 150-152 and 162-167 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. This rejection is respectfully traversed.

The invention as claimed is directed to a method of effecting change in the surface antigens expressed by a multi-cellular structure. The method comprises the step of contacting a suspension of the cell or multi-cellular structure with a synthetic molecule construct of the structure F-S_1-S_2-L for a time and at a temperature sufficient to effect the change. In the structure F-S_1-S_2-L, F is a glycotope, S_1 is a C_{3-5}-aminoalkyl selected from 3-aminopropyl, 4-aminobutyl, or 5-aminopentyl; S_2 is selected from -$CO(CH_2)_3CO$-, -$CO(CH_2)_4CO$- (adipate) and -$CO(CH_2)_5CO$- ; and L is a lipid selected from diacyl- and dialkyl-glycerophospholipids. Basis for the amended claims is detailed in Section IV of this Amendment.

The invention as claimed is described in the application in such a way as to reasonably convey that the inventors were in possession of the claimed invention at the time of filing of the application. Thus, as stated at page 17, line 16 of the specification:

> "The synthetic molecule constructs of the invention spontaneously and stably incorporate into a lipid bi-layer, such as a membrane, when a solution of the molecule is contacted with the lipid bi-layer. Whilst not wishing to be bound by theory it is believed that the insertion into the membrane of the lipid tails of the lipid (L) is thermodynamically favoured. Subsequent dissociation of the synthetic molecule construct from the lipid membrane is believed to be thermodynamically unfavoured. Surprisingly, the synthetic molecule constructs identified herein have also been found to be water soluble."

Furthermore, it is stated at page 17, line 35 of the specification that:

> "The synthetic molecule constructs of the invention comprise an antigen (F) linked to a lipid portion (or moiety) (L) via a spacer (S_1-S_2). The synthetic molecule constructs can be prepared by the condensation of a primary aminoalkyl, secondary aliphatic aminoalkyl or primary aromatic amine derivative of the antigen with an activated lipid. Methods of preparing neoglycoconjugates have been reviewed (Bovin, N. Biochem. Soc. Symp., 69,143-160).

Based on the above, it is clear that the inventors were clearly in possession of the invention as now claimed. The statements at, for example, page 18, line 36 to page 19, line 20 of the specification provide further evidence that the inventors were in possession of the claimed invention.

The Action states on page 4:

> "Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim."

Again, on page 4 of the Action, it is stated:

"If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within the genus."

In response, as stated at page 18, lines 36 onwards of the specification:

"The inventors have determined that to prepare synthetic molecule constructs of the invention where the antigen F is an oligosaccharide selected from the group of glycotopes for A-, B- and H- antigens of the ABO blood groups, the primary aminoalkyl, secondary aliphatic aminoalkyl or primary aromatic amine, and the activator should be selected to provide a spacer (S_1-S_2) with a structure according to one of those presented [in the Table provided at the top of page 19].

The structure of the spacer (S_1-S_2) is clearly defined in the Table. The specification goes on to describe variations in the genus at page 19, lines 3 to 20.

The Action further states on page 5:

"The claims herein are drawn to the use of any agents represented by "F-S_1-S_2-L" wherein F is a carbohydrate and S_1 and S_2 are spacer groups. <u>These are not further defined in the specification</u>." (Emphasis added).

This is not correct. The claimed method is limited to the use of a synthetic molecule construct including the spacer (S_1-S_2) as defined in the specification, for example in the Table at the top of page 19 of the specification (see also, the quote above at page 18, lines 3 6 onwards of the specification). The Action also confirms on page 6 that:

"The skilled artisan would also understand that, within that large number of combinations, are a number of embodiments of immense structural variation that would not be suitable for the claimed method, given the fact that any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physical, chemical, physiological effects and functions."

The claimed method uses a selection of synthetic molecule constructs with the properties required to effect changes in the surface antigens expressed by a cell or multi-cellular structure. These properties are discussed in the passages referred to above, and specifically at page 34, lines 36 to 40 of the specification where it is stated:

> "As described herein not all structures of the spacer (S_1-S_2) will provide a synthetic molecule construct (F-S_1-S_2-L) that is water soluble and spontaneously and stably incorporate in to a lipid bilayer such as a cell membrane. The synthetic molecule constructs designated A_{tri}-sp-lipid (IV) and Atri-PAA-DOPE (V) were determined not to be water soluble and/or unable to spontaneously and stably incorporate in to a lipid bilayer such as a cell membrane." (Emphasis in the original).

The meanings of the phrases *water soluble* and *stably incorporate* in this context are provided at page 18, lines 15 to 23 of the specification.

The Action states at page 6:

> "Although the claims may recite some functional characteristics, the claims lack written description because there is no correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification."

This statement is also incorrect. As evidenced by the passages referenced above and elsewhere in the specification, the correlation between function and structure has been clearly elaborated both with reference to the use of the genus and exemplifying species.

Based on the above, it is clear that the claimed invention is supported by an adequate written description. Withdrawal of the written description rejection is respectfully requested.

III. THE ENABLEMENT REJECTION

Claims 141-148, 150-153 and 162-167 stand rejected under 35 U.S.C. §112, first paragraph, on alleged lack of enablement grounds. The Action acknowledges that the specification is enabling for the use of the particular constructs (species) disclosed.

The claims stand rejected under 35 U.S.C. §112, first paragraph on alleged lack of enablement grounds. In response, the specification is similarly enabling for use of the genus as defined in Claim 141.

In support of this submission we reiterate the statements made a page 19, lines 3 to 20 of the specification.

Constructs of the genus as defined in Claim 141 are prepared by the reaction of an activated lipid (A-L) and an aminoalkyl glycoside as exemplified at page 49, line 16 to page *51*, line 21 of the specification.

Withdrawal of the lack of enablement rejection is respectfully requested.

IV. CLAIM AMENDMENTS

As noted earlier, the claims have been replaced by new claims 168-189. New claim 168 is based on previous claim 141 except that, in new claim 168, the definition of the moiety F of the construct (F-S_1-S_2-L) has been limited to a glycotope. Support appears in prior dependent claim 147. Furthermore, in new claim 168, the definitions of the moieties S_1 and S_2 of the construct (F-S_1-S_2-L) have been supplied (supported by previous claims 152 and 151, respectively).

The limitation in previous claim 141 that the construct includes the substructure as defined in claim 141 is now the subject of new claim 169. The definition of the

substructure provided in new dependent claim 169 has been amended to exclude the option of X being C and to include M as a monovalent cation that is typically H, but may be replaced by another monovalent cation such as Nat, K+ or NH_4+. Support for these amendments appears in the structures defined in prior claims 153 and 155 to 161. Dependent claim 178 is new and defines the limitation that the glycerophospholipid is 1,2-O-dioleoyl-sn-glycero-3-phosphatidylethanolamine (DOPE) or 1,2-O-distearyl-sn-glycero-3-phosphatidylethanolamine (DSPE). Support appears in original claim 5. The structures of the constructs provided in new dependent claims 180 – 186 have been amended to include the hydroxyl substituent previously omitted.

No new matter is entered by the requested amendments. Subject matter deleted by this Amendment has been canceled without prejudice to pursuing that subject matter in a separate continuing application.

V. MISSING REFERENCE

The document "Derwent Abstract Accession No. 2004-449665142 A25 B04 (A96)" mentioned on page 3 of the Action is attached hereto. Entry and consideration of this document are respectfully requested.

Favorable action is awaited.

BOVIN et al
Appl. No. 10/593,829
November 24, 2008

Respectfully submitted,

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Attachment: Derwent Abstract Accession No. 2004-449665142 A25 B04 (A96)

L1 ANSWER 1 OF 1 WPINDEX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-449665 [42] WPINDEX Full-text
CR 2005-603243
DNC C2004-168506 [42]
TI Liposome for improving residential time of anti-tumor agent in blood, comprises polyalkylene glycol coupled with albumin
DC A25; A96; B04
IN AZUMA Y; HIGAKI K; KAI T; KIMURA T; SATO M; YOKOE J; OGAWARA K; SAKURAGI S
PA (NIPR-N) NIPRO CORP; (AZUM-I) AZUMA Y; (HIGA-I) HIGAKI K; (KAIT-I) KAI T; (KIMU-I) KIMURA T; (SATO-I) SATO M; (YOKO-I) YOKOE J
CYC 105
PIA WO 2004045583 A1 20040603 (200442)* JA 56[7] <--
AU 2003280761 A1 20040615 (200470) EN
EP 1568360 A1 20050831 (200561) EN
JP 2004553161 X 20060316 (200620) JA 31
CN 1711074 A 20051221 (200636) ZH
KR 2005071641 A 20050707 (200643) KO
US 20060141019 A1 20060629 (200643) EN
ADT WO 2004045583 A1 WO 2003-JP14405 20031112; AU 2003280761 A1 AU 2003-280761 20031112; CN 1711074 A CN 2003-80103234 20031112; EP 1568360 A1 EP 2003-772728 20031112; EP 1568360 A1 WO 2003-JP14405 20031112; JP 2004553161 X WO 2003-JP14405 20031112; JP 2004553161 X JP 2004-553161 20031112; KR 2005071641 A WO 2003-JP14405 20031112; US 20060141019 A1 WO 2003-JP14405 20031112; KR 2005071641 A KR 2005-707490 20050429; US 20060141019 A1 US 2005-534874 20051215
FDT AU 2003280761 A1 Based on WO 2004045583 A; EP 1568360 A1 Based on WO 2004045583 A; JP 2004553161 X Based on WO 2004045583 A; KR 2005071641 A Based on WO 2004045583 A
PRAI JP 2002-332825 20021115
AN 2004-449665 [42] WPINDEX Full-text
CR 2005-603243
AB WO 2004045583 A1 UPAB: 20060121
NOVELTY - A liposome comprises polyalkylene glycol coupled with albumin.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a pharmaceutical composition contains the above liposome;
(2) treatment of cancer, which involves administering liposome containing polyalkylene glycol coupled with albumin and an anti-tumor agent;
(3) use of liposome containing polyalkylene glycol coupled with albumin for extending the residential time of biologically active component in the living body of the liposome containing biologically active component; and
(4) manufacture of liposome, which involves combining compounds of formulae 1-8.
R = 2-35 acyl fatty acid;
Alb-NH = the group formed by removing one hydrogen atom of the amino group from the albumin molecule Alb-NH2; and
n = 5-100000.
ACTIVITY - Cytostatic.
No suitable biological data given.
MECHANISM OF ACTION - None Given.
USE - For improving residential time of anti-tumor agent in blood (claimed) for treating cancer, tumor, colon cancer, brain tumor, head and neck cancer, breast cancer, lung cancer, oesophageal cancer, stomach cancer, hepatic carcinoma, gall bladder cancer, cholangiocarcinoma, pancreatic cancer, islet cell cancer, bladder cancer, testis cancer, prostatic cancer, orchioncus, ovarian cancer, uterine cancer, choriocarcinoma, thyroid cancer, malignant carcinoid tumor, skin cancer, malignant melanoma, osteosarcoma, soft structure sarcomata, neuroblastoma, Wilms tumor, retinoblastoma, melanoma and squamous cell carcinoma.
ADVANTAGE - The liposome has improved retention properties in blood. The liposome has synergistic effect for improving the residential time of active component in blood. The liposome containing polyalkylene glycol coupled with albumin is manufactured easily.

DESCRIPTION OF DRAWINGS - The figure shows graphical representation of variation in time course of blood level of liposome. (Drawing includes non-English language text).